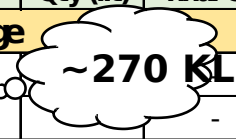
Contents

1. Spent solvent streams at LS3.
2. Spent Solvent Transfer Philosophy.
3. Distilled Solvent Transfer Philosophy.
4. Transfer Philosophy Pictorial.
5. Proposed P&ID.
6. Proposed SRS Tank Pad Layout.
7. Points to be discussed.
8. Additional SOP’s for SRS Operations apart from Production.

Spent Solvent Streams at LS3 (N-1 & Pharma Streams way forward to be discussed)

Spent Solvent generation Details at LS-III														
S.no	Product name	Stage code		Batch size (kg)	No'of Batches/ Month	Solvent name	Total input / Batch (lit)	Spent Genaration/ Batch			After treatment final Qty	Spent Genaration / month	After Tretment Analysis		
								Distilled Qty (lit)	O.L Qty (lit)	C.F ML'S Qty (lit)			G.C. Analysis	MC	pH
Up to N-2 Stage															
1	Pregabalin	AMHA1	**N-3**	862	35	**Methanol**	3450	2000	-			70000	88%MeOH & 9.9%Unknown(TOL)	10.8%	1.97
2	Pregabalin	AMHA12C EA	**N-3**	1450	7	**Methanol**	3200	1750	-		-	12250	91.39% MeOH & 5.48 Unknown(TOL)	7.20%	1.35
3	Pregabalin	AMHA12C M-470	**N-3**	1450	6	**Methanol**	3120	1700	-	-	-	10200			
4	Clopi	COPB1	**N-2**	700	14	**Methanol**	4424	-	-	4000	3300	46200	73.85%MeOH & 18.43%Acetone	1.0%	8.41
5	Levetracitam	LVTA2	**N-2**	350	10	**Methanol**	1200	1000	-	-	-	10000	93.15%MeOH & 6.85%EA	0.7%	10.69
6	Levetracitam	LVTA2	**N-2**	225	15	**E.A.**	2275	-	-		1800	27000	68.12%EA & 28.19%MeOH	0.71%	9.84
N-1 Stage															
1	Clopi	CGBH1	**N-1**	500	27	**Ethyl Acetate**	2200	-	-		1700	45900	89.62%EA & 10.38%IPA	5.47%	5.5
2	Levetracitam	LVTC1	**N-1**	225	26		450	350	-	-	-	9100	88.64 %E.A. & 6.4%MDC	1%	8.7
3	Levetracitam	LVTC1	**N-1**	225	26		675	-	-	450	370	9620	96.75%E. A. & 3.25%MDC	0.86%	
4	Rosuvastatin Ca	RSC2B	**N-1**	150	15		5500	-	-	5500	4400	66000	97.8%E. A. & 2%IPA	4.50%	
5	Clopi	CGBH1	**N-1**	500	27	**IPA**	1800	-	-	1600	1200	32400	83.38 %IPA & Unknown (Tol)- 16.37%	9.98%	5.74
6	Vildagliptin	VGPT1	**N-1**	160	8		360	-	-	400	275	2200	89.73%IPA & 5.9%MTBE	1%	
7	Rosuvastatin Ca	RSC2B	**N-1**	150	15		750	760	-	-	-	11400	Purity- 94%	20%	~9-10
8	Vildagliptin	VGPT1	**N-1**	160	8	**MDC**	1260	600	-			4800	MDC- 77.79%& Unknown- 22.21%	0.38	3.38
Pharma Stage															
1	Clopi	CGBH2	**Pharma**	500	19	**Acetone**	3000	-	-	2600	2400	45600	Acetone: 99.04%& Unknown (CH)- 1.96%	3.58%	9.31
2	Vildagliptin	VGPT2	**Pharma**	250	4		1250	700	-	-	-	2800	98%Acetone & 1.5%Unknown	~1.5%	
3	Levetracitam	LVTC2	**Pharma**	220	26	**Ethyl Acetate**	1760	-	-	1600	1500	39000	97%E.A. & 3%Methanol	0.85%	8.04
4	Levetracitam	LVTC2	**Pharma**	220	26		440	380	-	-	350	9100	92%E.A & & 8%Methanol	0.85%	8.04
5	Vildagliptin	VGPT2	**Pharma**	250	4		500	300	-	-	-	1200	85%E. A. & 13%Methanol	1%	
6	Vildagliptin	VGPT2	**Pharma**	250	4		1000	-	-	950	650	2600	94%E. A. & 5%Methanol	1%	
7	Levetracitam	LVTC2	**Pharma**	220	10	**Methanol**	1600	1200	-	-	-	12000	98%Methanol & 1.5%E. A.	1%	
8	Vildagliptin	VGPT2	**Pharma**	250	4		875	650	-	-	-	2600	96%Methanol & 3%MDC	1.5%	
9	Vildagliptin	VGPT2	**Pharma**	250	4	**MDC**	1200	-	1050	-	1200	4800	80%MDC Unknown- 19.55%	1.5%	NA
10	Vildagliptin	VGPT2	**Pharma**	250	4		850	550	-	-		2200			



Spent Solvent Transfer Philosophy:

Manufacturing Block to Production Tank Pad

- Permanent lines for Dedicated Streams (4 Lines).
- HDPE Drums/ containers for campaign based solvents.

Production Tank Pad to SRS Tank Pad

- Permanent lines for Dedicated Streams (4 Lines).
- Road Tanker for Campaign based solvents from LS3/ Other Units.

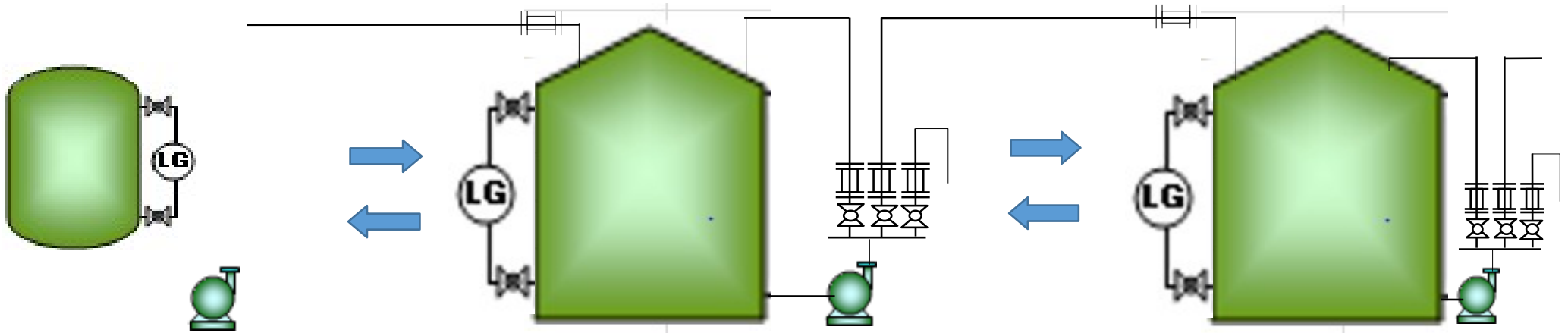
SRS Tank Pad to Column

- Permanent Lines

Distilled Solvent Transfer Philosophy:

SRS to SRS Tank Pad	• Permanent Lines
SRS Tank Pad to Production Tank Pad	• Permanent lines for Dedicated Streams (2 Lines). • Road Tanker for Campaign based solvents from LS3/ Other Units.
Production Tank pad to manufacturing Block	• Permanent lines for Dedicated Streams (2 Lines) • HDPE Drums/ containers for campaign based solvents

Permanent Lines Planning for Dedicated Streams

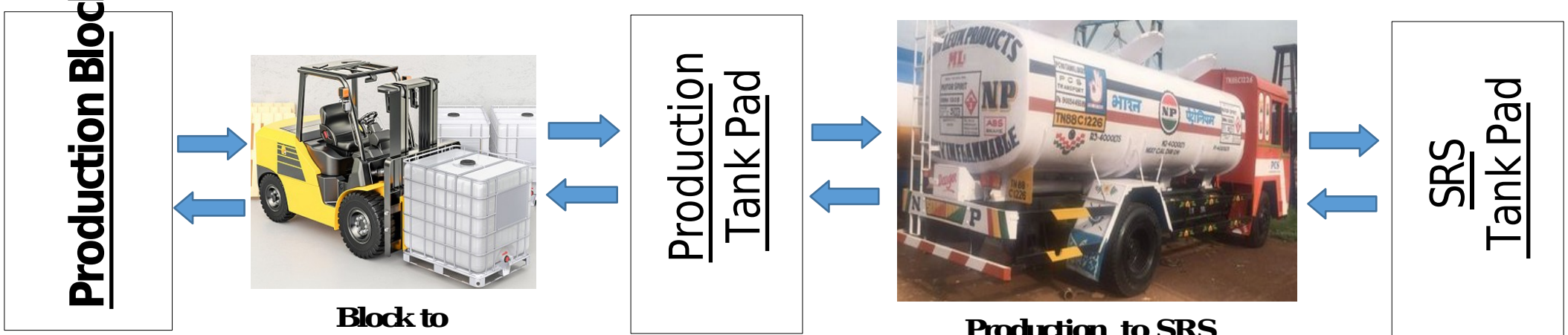


Receier at Production Block

30KL at Spent/ 10KL distilled Tank at Production Tank Pad

30KL at Spent Tank at SRS

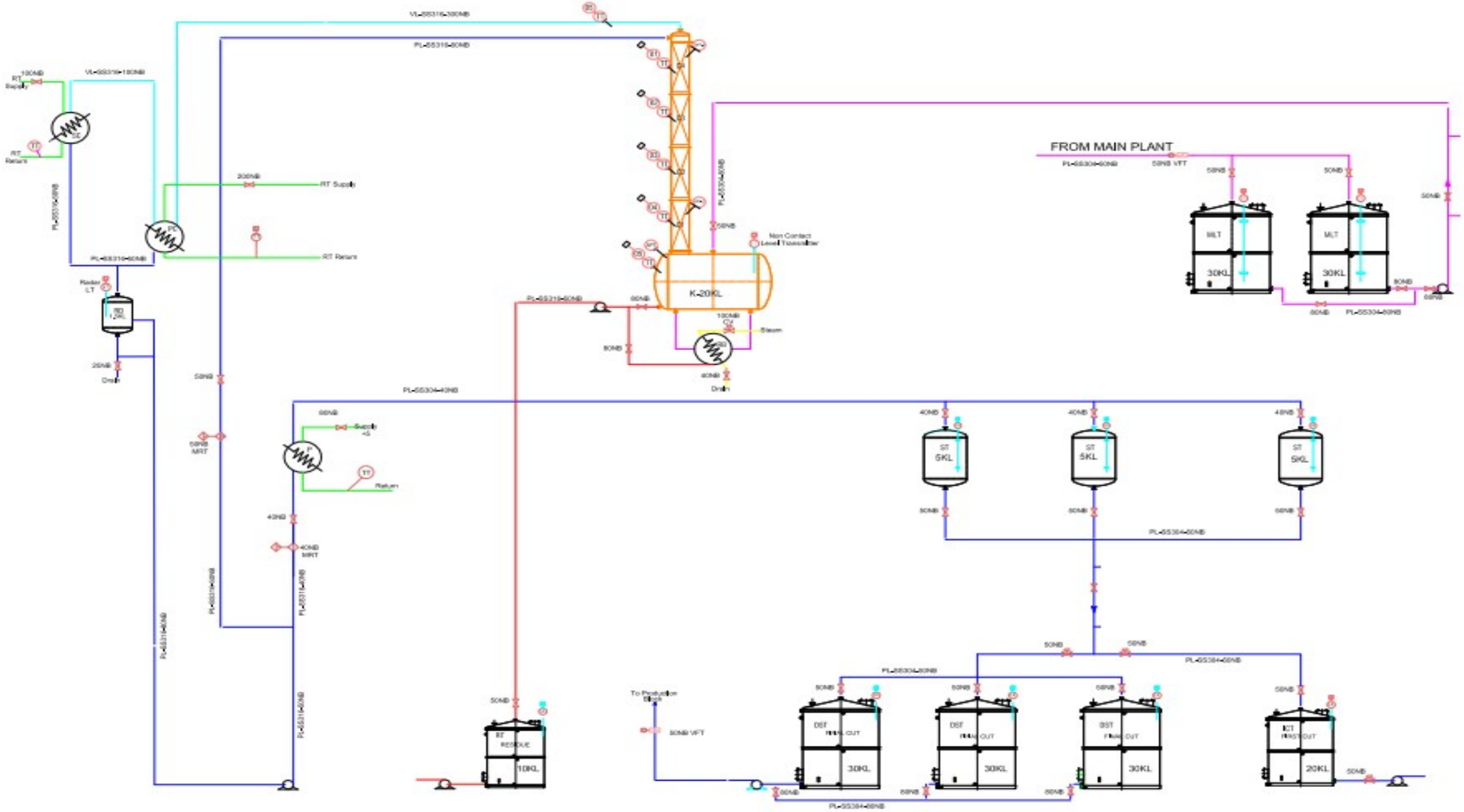
Other Campaign Based Streams Planning with Rad Tanker



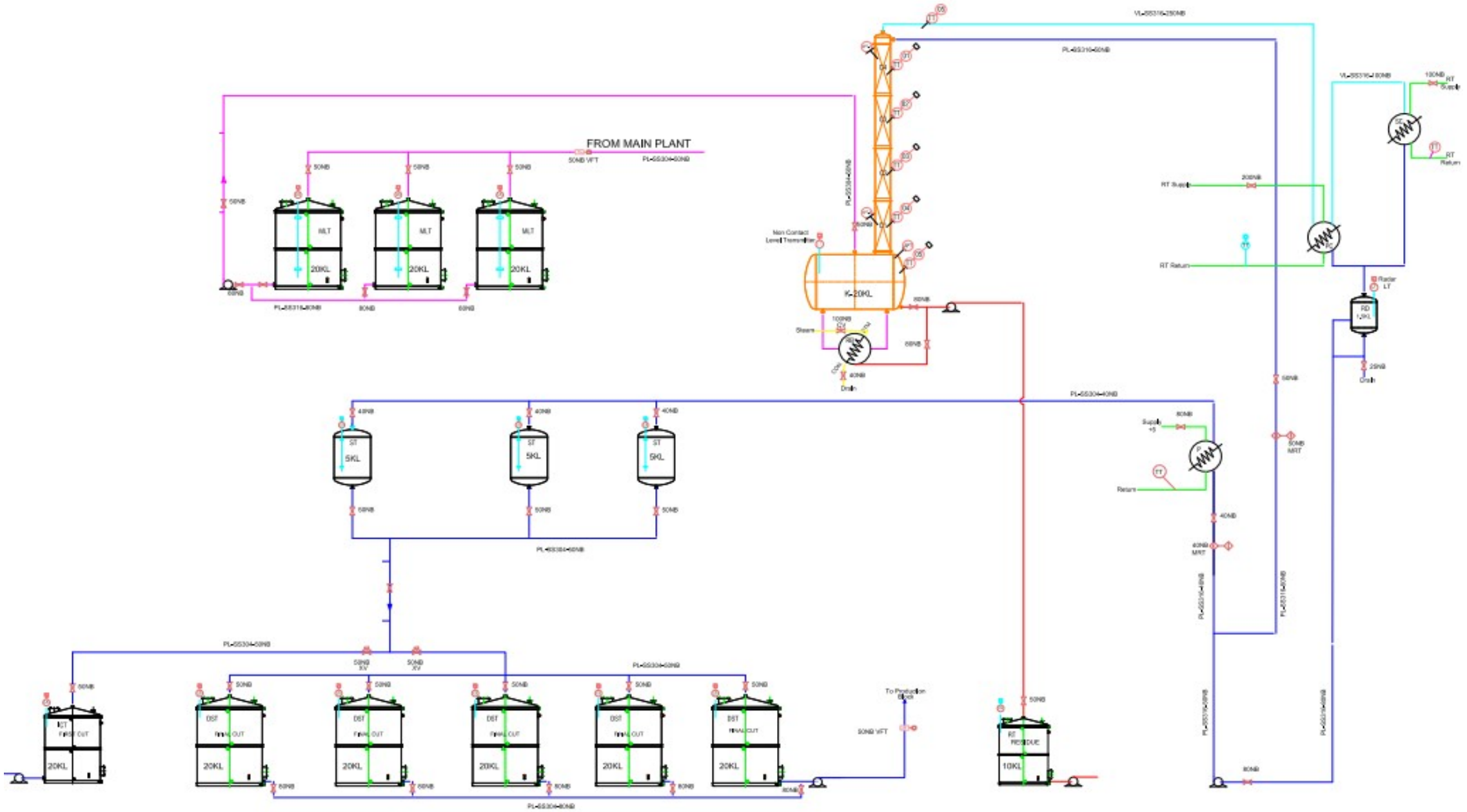
Block to Production tank pad with Fork lift

Production to SRS tank pad with Road Tanker

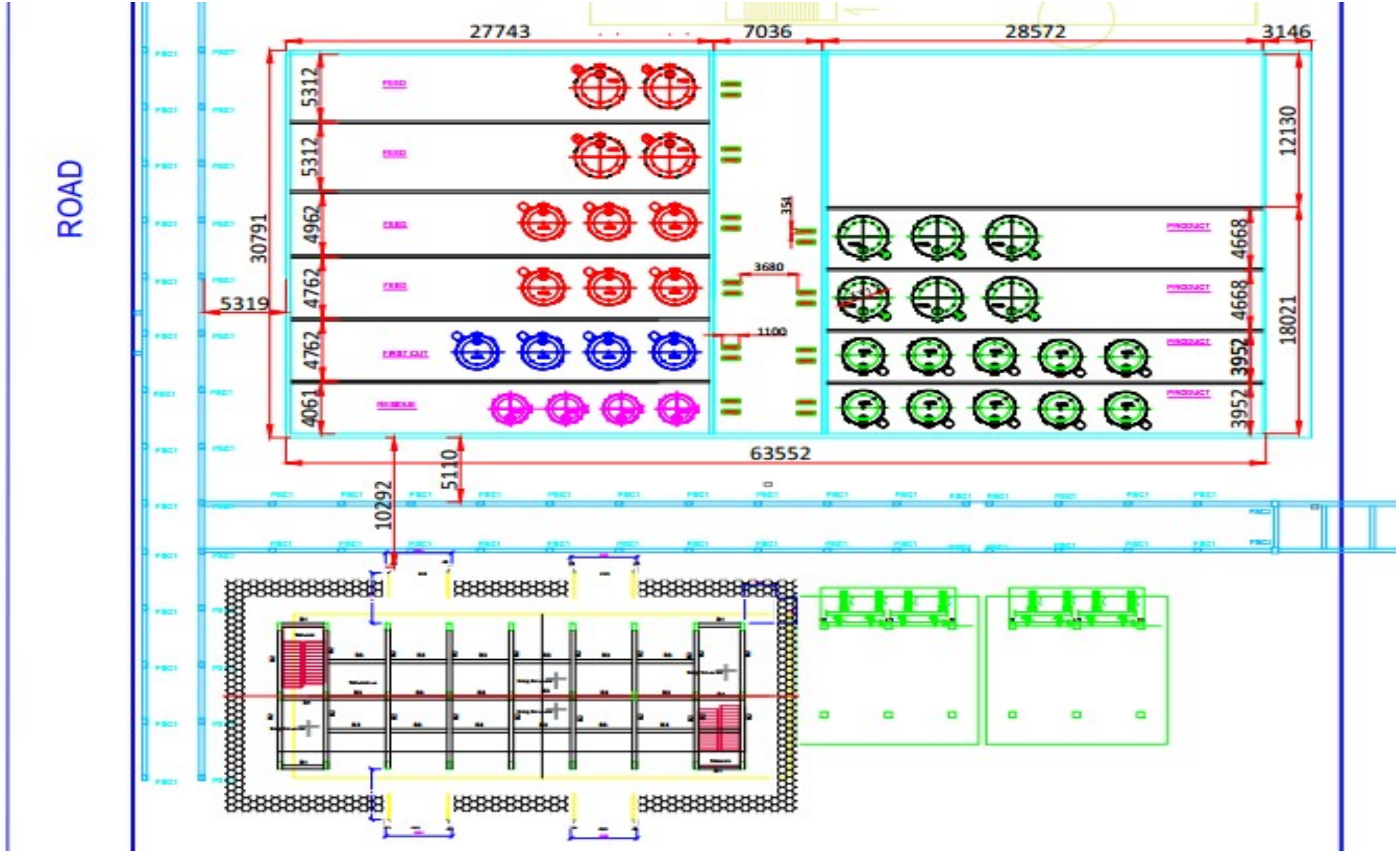
Proposed P&ID for Ø 900 Column:



Proposed P&ID for Ø 750 Column:



Proposed Layout for SRS Tank Pad:



Points to be discussed:

Production:

- Additional SOPs apart from existing Production SOP’s.
- Trial & Validation requirement- Validation master plan, Protocol, Process, BPR, BCR
- Road tanker for Spent/ distilled solvent transfer:
  - Dedicated road tankers required, one for spent and other for distilled solvents.
  - Road tanker cleaning procedure to be established.
  - Cleaning sample analysis will be checked at cleaning validations, next onwards will be cleaned with road tanker cleaning checklist without analysis.
- Product or solvent Change over cleaning:
  - Changeover cleaning procedure to be established for **Distillation column, spent tanks, distilled tanks, road tanker**.
  - Permanent transfer lines cleaning procedure to be finalised- (Nitrogen flushing, followed by holdup unloading from drain points in-between)
  - Is cleaning required for change-over of same solvent in different stage of same product?
- Dedicated manpower for above documentation activities with relevant experience/ exposure in SRS area.

Points to be discussed:

Quality:

- Nitrosamine risk assessment for recovery solvents.
- R&D procedure for BPR preparation.
  - 10 Lts. lab column experiments accepted or not?.
- In-process samples and final distilled solvent- specification and MOA development.
- Target Specification of distilled solvent- shall match with fresh solvent or not?
- For Azeotropic mixtures (IPA+ Water, Methanol+ Acetone etc.) can we use in process as such with quantification?
- Any Special quality parameters apart from GC, MC, pH etc. (like ROI etc.)
- Dedicated Streams or mixture of streams:
  - mixture of same solvent from all stages of same product.
  - mixture of same solvent from different product.
- Can we use Distilled solvents from Campaign based products in other products?
- Risk Assessment for usage in other products.
- SRS QC Laboratory (GC, Water content, pH etc.)
  - Location and Instruments Qualifications &
  - Dedicated Manpower

Points to be discussed:

Engineering:

- Color coding for Spent and Distilled solvents
  - White color band on same solvent color code.
  - Color coding difficult for Campaign based streams.
- URS and CCF Initiation before PR- Target date _____.
- Location to be finalised for following
  - Utilities Block & Panel Room.
  - HMI & Office room.
  - Permanent location of SRS Lab for 10 lt. glass column installation.
  - SRS QC Lab.

Additional SOP’s for SRS Operations apart from Production:

- Indent, receipt, Storage, and usage of Raw materials.
- Operation of Column and Kettle
- Cleaning of column and kettle
- Application of Utilities.
- Receivers & Storage Tanks Cleaning.
- Cleaning of spilled solvents.
- Earthing connection to hose and drums while transferring solvents.
- Cleaning of empty drums.
- In process sampling.